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EXAMINER	
ROMEO, DAVID S	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 02/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/014,162	USDIN ET AL.	
	Examiner	Art Unit	
	David S Romeo	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If the period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 November 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *5,6,10-17 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4 and 7-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-19* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 November 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *0802*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election of group I, claims 1-9, 18, and the species SEQ ID NO: 1 in the reply filed on 11/19/2004 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 3-6, 18 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/19/2004.

Claims 10-17, 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 11/19/2004.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Brewer (B) in view of Usdin (9, cited by Applicants).

Brewer discloses isolated or purified PTH (Abstract). Usdin discloses that hPTH-(1-34) is a PTH2 receptor ligand (first sentence of paragraph bridging pages 15456-

15457). Accordingly, Brewer discloses an isolated or purified peptide that is a PTH2 receptor ligand.

Claims 1, 2, 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Usdin (12, cited by Applicants).

Usdin (12) discloses a partially purified hypothalamic extract (page 831, right column, full paragraph 1). The receptor selectivity and chromatographic behavior of the activity in the hypothalamic extract suggest that it is a polypeptide acting at cell surface PTH2 receptors (page 833, right column, full paragraph 1). Usdin's (12) experiments provide evidence for a peptide acting at the PTH2 receptor in extracts prepared form bovine hypothalamus. The receptor selectivity and immunological properties of the PTH2 receptor activating material in the hypothalamic extract demonstrate that it is not PTH. See paragraph bridging pages 833-834. If the material activates the PTH2 receptor at a similar concentration to synthetic PTH then there are approximately 100nmoles of the polypeptide per 50 hypothalami. Study of the role of this potential new neurotransmitter will be facilitated by determination of its sequence, and purification or synthesis of larger quantities. See page 834, left column, full paragraph 1.

In the present application the amino acid sequence of SEQ ID NO: 1 was obtained by purification of the PTH2 receptor ligand found in bovine hypothalamus extract. See Example 6.

Therefore, Usdin's (12) peptide appears to be identical with the claimed peptide, i.e., both were obtained from the same source and both bind the same receptor. The limitations "isolated" and "purified" in the present claims do not distinguish the presently

claimed peptide from Usdin's (12) peptide. Determination of the amino acid sequence of Usdin's (12) peptide merely amounts to a further characterization of a peptide which is already described in the prior art. The identification and characterization of a prior art material also does not make it novel. The burden is on applicant to show a novel or unobvious difference between the claimed peptide and Usdin's (12) peptide.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 2, 7, 8, 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Usdin (12, cited by Applicants) in view of Usdin (9, cited by Applicants), Park (A) and Angal (U).

Usdin (12) discloses a partially purified hypothalamic extract (page 831, right column, full paragraph 1). The receptor selectivity and chromatographic behavior of the activity in the hypothalamic extract suggest that it is a polypeptide acting at cell surface PTH2 receptors (page 833, right column, full paragraph 1). Usdin's (12) experiments provide evidence for a peptide acting at the PTH2 receptor in extracts prepared form bovine hypothalamus. The receptor selectivity and immunological properties of the PTH2 receptor activating material in the hypothalamic extract demonstrate that it is not PTH. See paragraph bridging pages 833-834. If the material activates the PTH2 receptor at a similar concentration to synthetic PTH then there are approximately 100nmoles of

the polypeptide per 50 hypothalami. Study of the role of this potential new neurotransmitter will be facilitated by determination of its sequence, and purification or synthesis of larger quantities. See page 834, left column, full paragraph 1.

In the present application the amino acid sequence of SEQ ID NO: 1 was obtained by purification of the PTH2 receptor ligand found in bovine hypothalamus extract. See Example 6.

Therefore, Usdin's (12) peptide appears to be identical with the claimed peptide, i.e., both were obtained from the same source and both bind the same receptor. The limitations "isolated" and "purified" in the present claims do not distinguish the presently claimed peptide from Usdin's (12) peptide. Determination of the amino acid sequence of Usdin's (12) peptide merely amounts to a further characterization of a peptide which is already described in the prior art. The identification and characterization of a prior art material also does not make it novel. The burden is on applicant to show a novel or unobvious difference between the claimed peptide and Usdin's (12) peptide.

Usdin (12) does not teach in the sense that Usdin (12) does not anticipate an isolated or purified complex comprising the PTH2 receptor and a PTH2 ligand comprising the amino acid sequence of SEQ ID NO: 1.

Usdin (9) teaches a cDNA clone encoding the PTH2 receptor and its amino acid sequence (page 15455, right column, full paragraph 1, through paragraph bridging pages 15455-15456; Figure 1).

Park is evidence that it was known in the art at the time of Applicants' invention to use receptors as binding agents for affinity purification procedures of binding ligands (column 7, lines 50-64).

Angal teaches that, at best, affinity chromatography is the most powerful technique for protein purification, allowing purification of a single protein of low abundance from a crude mixture of proteins at higher concentrations. If the affinity of the ligand for the protein is sufficiently high, the technique offers simultaneous concentration from a large volume. See page 245, last paragraph of "Introduction".

Usdin (9), Park, and Angal do not teach an isolated or purified complex comprising the PTH2 receptor and a PTH2 ligand comprising the amino acid sequence of SEQ ID NO: 1.

However, it would have been obvious to one of ordinary skill in the art at the time of Applicants' invention to make an isolated or purified peptide that is a PTH2 receptor ligand, as taught by Usdin (12), and to modify that teaching by using the PTH2 receptor, as taught by Usdin (9), for the affinity purification of its ligand, as taught by Park, with a reasonable expectation of success. One of ordinary skill in the art would be motivated to make this modification because Usdin (12) suggest purification of larger quantities of the PTH2 receptor ligand and because, at best, affinity chromatography is the most powerful technique for protein purification. In carrying out affinity chromatography with Usdin's (9) PTH2 receptor and Usdin's (12) PTH receptor ligand, one of ordinary skill in the art would obtain an isolated or purified complex comprising the PTH2 receptor and a PTH2 ligand comprising the amino acid sequence of SEQ ID NO: 1. One of ordinary skill in the art would also further purify or isolate the already purified or isolated PTH2 receptor ligand of Usdin (12). Claims 1, 2, and 7 are included in this rejection in the event that Applicants' show that the "isolated" or "purified" limitations in the present claims distinguish over Usdin's (12) isolated or purified PTH2 receptor ligand, and thus

overcome the rejection under 35 U.S.C. § 102(b) over Usdin (12) above. The invention is prima facie obvious over the prior art.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3, 7, 8 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1 and 8 are directed to or encompass the genus of any and/or all peptides that are PTH2 receptor ligands. Claim 3 encompasses the genus of any and/or all peptides at least 39 amino acids in length that are PTH2 receptor ligands. No common structural attributes identify the members of the genus in claim 1, 3, or 8. Structural features that could distinguish compounds in the genus from others in the protein class are missing. Claim 7 is directed to a genus of peptides at least 70% identical to SEQ ID NO: 1. No common functional attributes identify the members of the genus in claim 7. Functional features that could distinguish compounds in the genus from others in the protein class are missing.

The present specification discloses that a search of GenBank with the sequence of bovine TIP39 (SEQ ID NO: 107) identified a homologous sequence in a working draft

human genomic sequence, GenBank accession number AC068670 (SEQ ID NO: 108). The predicted amino acid sequence of the putative peptide encoded by this human DNA is identical to the sequence of bovine TIP39. See page 52, full paragraph 2. In other words, the disclosed bovine and human species are 100% conserved. There is no evidence of record that PTH2 receptor ligands are highly variant. However, the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. Because the genus is highly variant, SEQ ID NO: 1 alone is insufficient to describe the genus. It appears to be well settled that a single species can rarely, if ever, afford sufficient support for a generic claim. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus.

An applicant complies with the written description requirement by describing the invention, with all its claimed limitations, not that which makes it obvious, and by using such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention. Applicants must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, they were in possession of the invention. The specification does not clearly allow persons of ordinary skill in the art to recognize that Applicants invented what is claimed.

With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed peptides. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. Therefore, only SEQ ID NO: 1 but not the full breadth

of the claim meets the written description provision of 35 U.S.C. 112, first paragraph. Applicant is reminded that the written description provision of 35 USC 112 is severable from its enablement provision.

Claims 1, 3, 4, 7, 8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a peptide comprising the amino acid sequence of SEQ ID NO: 1, does not reasonably provide enablement for the PTH2 receptor ligand of claims 1, 3, 4, or 8 without regard to the structure thereof, or the peptide of claim 7 without regard to the functional activity thereof. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1 and 8 are directed to or encompass the genus of any and/or all peptides that are PTH2 receptor ligands. Claim 3 encompasses the genus of any and/or all peptides at least 39 amino acids in length that are PTH2 receptor ligands. No common structural attributes identify the members of the genus in claim 1, 3, or 8. The skilled artisan is left to an extensive amount of trial and error experimentation wherein peptides are randomly made and tested for the desired activity. Claim 7 is directed to a genus of peptides at least 70% identical to SEQ ID NO: 1. No common functional attributes identify the members of the genus in claim 7. The skilled artisan is left to an extensive amount of experimentation, wherein SEQ ID NO: 1 is randomly mutated, and through trial and error experimentation is left to determine how to use such peptides. Such extensive, random trial and experimentation is considered undue.

The present specification discloses that a search of GenBank with the sequence of bovine TIP39 (SEQ ID NO: 107) identified a homologous sequence in a working draft human genomic sequence, GenBank accession number AC068670 (SEQ ID NO: 108). The predicted amino acid sequence of the putative peptide encoded by this human DNA is identical to the sequence of bovine TIP39. See page 52, full paragraph 2. In other words, the disclosed bovine and human species are 100% conserved. There is no evidence of record that PTH2 receptor ligands are highly variant. Guo (V) teaches that evolutionarily conserved residues show low substitutability indices (Abstract). The effects of mutations on protein function are largely additive (page 9207, left column, full paragraph 2). Highly conserved proteins are likely to be relatively intolerant to mutation (page 9207, left column, last full paragraph). Therefore, the scope of the claimed variants is not representative of the scope of enablement provided by the specification.

The present specification also discloses that the N-terminal region of TIP39 is therefore a determinant of PTH2 receptor activation (page 57, full paragraph 1). Loss of the six N-terminal residues from TIP39 converts it from a PTH2 receptor agonist to a weak PTH2 receptor antagonist and a selective, high affinity PTH1 receptor antagonist (paragraph bridging pages 57-58). There are no working examples of PTH2 receptor ligand variants that are representative of the claimed variants that vary anywhere and everywhere from the amino acid sequence of SEQ ID NO: 1. The examiner is aware that working examples are not required. Lack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art. Claim 7 is broad because it does not require the claimed peptide to be identical to SEQ ID NO: 1 and because the claim has no functional limitation.

In view of the breadth of the claims, the limited amount of direction and working examples provided by the inventor, the unpredictability in the art and the quantity of experimentation needed to make or use the invention based on the content of the disclosure, it would require undue experimentation for the skilled artisan to make and/or use the full scope of the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 3 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 is indefinite over "one or more amino acid substitutions at positions" because it is unclear if a single amino acid is substituted by another single amino acid or if a single amino acid sis substituted by one or more amino acids. The metes and bounds are not clearly set forth.

Claim 3 is indefinite because prior to the "wherein" clause specific amino acids in the native sequence of SEQ ID NO: 1 are substituted with "U." In the "wherein" clause "U" is substituted. It is unclear how to construe the substitutions. The metes and bounds are not clearly set forth.

Claim Objections

Claims 3 and 4 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim.

Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. A peptide comprising a substitution in SEQ ID NO: 1 (claims 3 and 4) fails to further limit a peptide comprising SEQ ID NO: 1 (claim 2).

Drawings

New corrected drawings in compliance with 37 CFR 1.121(d) are required in this application because the different views are not numbered in consecutive Arabic numerals. Applicant is advised to employ the services of a competent patent draftsperson outside the Office, as the U.S. Patent and Trademark Office no longer prepares new drawings. The corrected drawings are required in reply to the Office action to avoid abandonment of the application. The requirement for corrected drawings will not be held in abeyance.

Applicants are advised that a further amendment to the specification correcting references to drawing figure(s) to correspond with the relabeled drawing figure(s), both in the brief and detailed descriptions of the drawings is required.

Specification

The disclosure is objected to because of the following informalities:

The application is not fully in compliance with the sequence rules, 37 C.F.R. § 1.821-1.825. Specifically, the specification fails to recite the appropriate sequence identifiers at each place where a sequence is discussed. The brief description of Figure I (page 3) and Figure I discuss sequences that are set forth in the "Sequence Listing." Reference must be made to the sequences by use of the sequence identifier, preceded by

"SEQ ID NO: " in the text of the description or figures. This is not meant to be an exhaustive list of places where the specification fails to comply with the sequence rules. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification. The application cannot issue until it is in compliance. Nucleic acid sequences with 10 or more nucleotides, at least 4 of which are specifically defined, must comply with the sequence rules. Amino acid sequences with 4 or more residues, at least 4 of which are specifically defined, must comply with the sequence rules. Sequence identifiers can also be used to discuss and/or claim parts or fragments of a properly presented sequence. For example, language such as "residues 14 to 243 of SEQ ID NO:23" is permissible and the fragment need not be separately presented in the "Sequence Listing." Applicant may bring the figure(s) into compliance by amending either the figure(s) or the "Brief Description of the Drawings" to recite the appropriate sequence identifier.

Appropriate correction is required.

Conclusion

No claims are allowable.

ANY INQUIRY CONCERNING THIS COMMUNICATION OR EARLIER COMMUNICATIONS FROM THE EXAMINER SHOULD BE DIRECTED TO DAVID S. ROMEO WHOSE TELEPHONE NUMBER IS (571) 272-0890. THE EXAMINER CAN NORMALLY BE REACHED ON MONDAY THROUGH FRIDAY FROM 7:30 A.M. TO 4:00 P.M. IF ATTEMPTS TO REACH THE EXAMINER BY TELEPHONE ARE UNSUCCESSFUL, THE EXAMINER'S SUPERVISOR, BRENDA BRUMBACK, CAN BE REACHED ON (571) 272-0961.

IF SUBMITTING OFFICIAL CORRESPONDENCE BY FAX, APPLICANTS ARE ENCOURAGED TO SUBMIT OFFICIAL CORRESPONDENCE TO THE CENTRAL FAX NUMBER FOR OFFICIAL CORRESPONDENCE, WHICH IS (571) 273-8300

CUSTOMERS ARE ALSO ADVISED TO USE CERTIFICATE OF FACSIMILE PROCEDURES WHEN SUBMITTING A REPLY TO A NON-FINAL OR FINAL OFFICE ACTION BY FACSIMILE (SEE 37 CFR 1.6 AND 1.8).

FAXED DRAFT OR INFORMAL COMMUNICATIONS SHOULD BE DIRECTED TO THE EXAMINER AT (571) 273-0890.

ANY INQUIRY OF A GENERAL NATURE OR RELATING TO THE STATUS OF THIS APPLICATION OR PROCEEDING SHOULD BE DIRECTED TO THE GROUP RECEPTIONIST WHOSE TELEPHONE NUMBER IS (703) 308-0196.

David Romeo

DAVID ROMEO
PRIMARY EXAMINER
ART UNIT 1647

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DSR
FEBRUARY 4, 2005